



P = .002

SPLEEN(S): SPLEEN CELLS FROM RATS TREATED WITH SALINE WHEN THEY WERE FETUSES.

 3 [H]-THYMIDINE INCORPORATION (cpm/106 Spleen Cells) 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6

HEP: IRRADIATED HUMAN HEPATOCYES.

SPLEEN(IU): SPLEEN CELLS FROM RATS TOLERIZED BY INTRAUTERINE INJECTION OF HUMAN HEPATOCYTE LYSATES.

SPLEEN(IU/IS): SPLEEN CELLS FROM RAT TOLERIZED BY INTRAUTERINE INJECTION OF HUMAN HEPATOCYTE LYSATES FOLLOWED BY INTRASPLENIC TRANSPLANTATION OF HUMAN HEPATOCYTES AFTER BIRTH.

HEP ALONE

2breen(In/I2)+Heb

SPLEEN(IU)+HEP

2b[EEN(2)+HEb

2PLEEN(S)+SPLEEN

2breen(s) arone

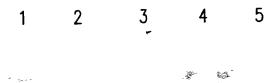
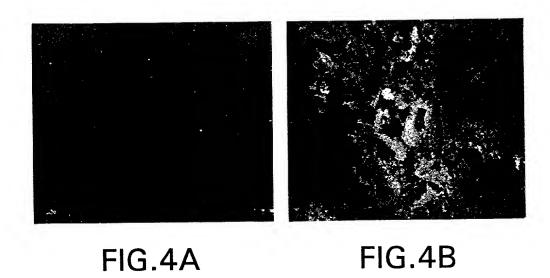
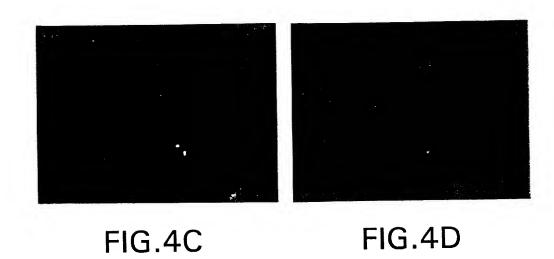


FIG.2

10 11 1 70 kD -60 kD -40 kD -1: Molecular weight markers 2: Human serum albumin, 50 ug 3: Human serum albumin, 10 ug 4: Human serum albumin, 1 ug 5: Week 1 post-human hepatocyte transplant 6: Week 2 post-human hepatocyte transplant 7: Week 3 post-human hepatocyte transplant 8: Week 4 post-human hepatocyte transplant 9: Week 5 post-human hepatocyte transplant 10: Control animal. human fibroblast transplant. 1 week 11: Rat serum albumin, 50 ug

FIG 3





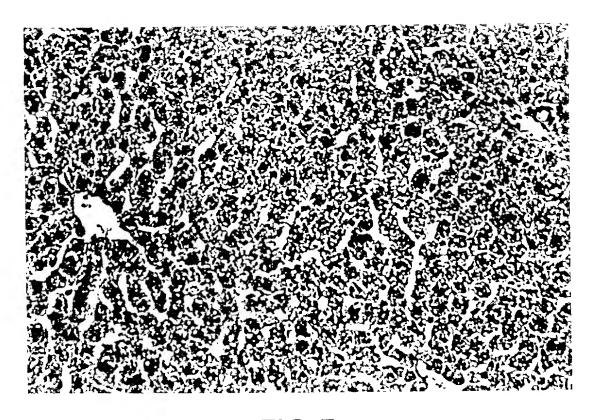


FIG.5

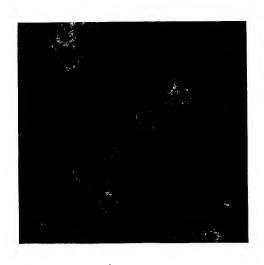


FIG.6A

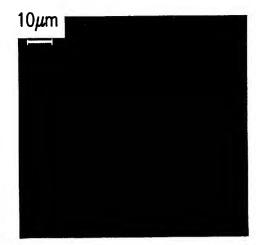


FIG.6B

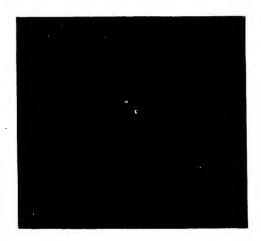


FIG.6C

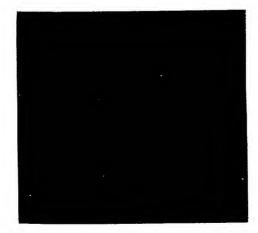


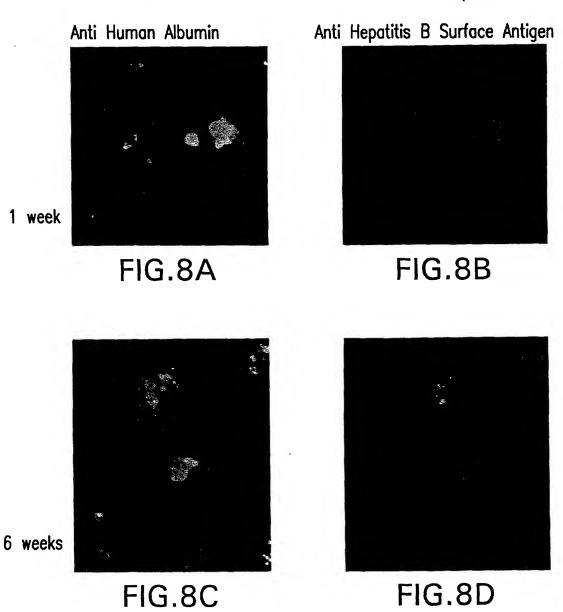
FIG.6D

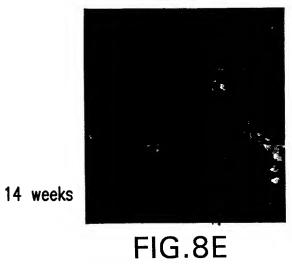
1 2 3 4 5 6 7 68,000 -

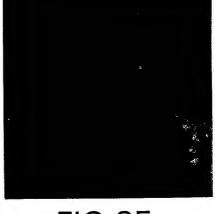
- 10 ng standard human albumin 10 ng standard rat albumin 2 days 2 weeks 1:
- 2:
- 3:
- 4:
- 5: 3 weeks
- 5 weeks 6:
- 7: 6 weeks

FIG.7

Time course of human albumin and HBV expression







G.8E FIG.8F

Anti Human Albumin

FIG.9A

Anti Hepatitis B Surface Antigen



FIG.9B

Rat CA3 Hepatocytes alone

Rat CA2

Hepatocytes Plus HBV



FIG.9C

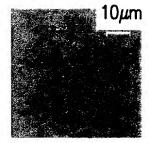
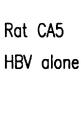


FIG.9D



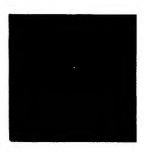


FIG.9E

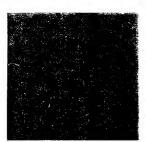
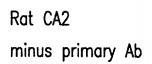


FIG.9F



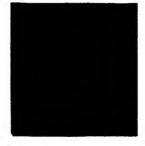


FIG.9G

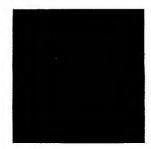
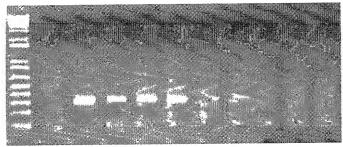


FIG.9H

RT-PCR Human Albuman mRNA

3 10 11 1 2



400 bp -300 bp -

- 1: 1000 bp ladder
- 2: Rat RÑA
- 3: Human RNA

- 3: Human RNA
 4: HepG2.2.15 RNA
 5: Rat CA1 Human hepatocytes + HBV
 6: Rat CA2 Human hepatocytes + HBV
 7: Rat CA3 Human hepatocytes
 8: Rat CA4 Human hepatocytes
 9: Rat CA5 HBV
 10: Rat CA6 HBV
 11: Rat CA7 Saline

FIG 10

RT-PCR Human Albumin RNA

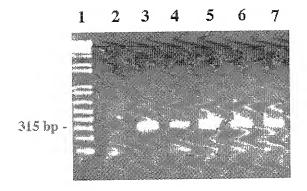


FIG 11A

RT-PCR HBV RNA

7 5 б Table 1 2 3 355 bp -

- 1: 1 kbp ladder
 2: Rat liver RNA
 3: Human liver RNA
 4: HepG2.2.14 RNA
 5: Rat CA2 Human hepatocytes +HBV, 1 week post
 6: Rat CA2 6 weeks post
 7: Rat CA2 14 weeks post

FIG 11B



- 1000 bp ladder 1:
- 2: Rat RNA
- 3: Human RNA
- HepG2.2.15 RNA 4:
- Rat CA1 Human hepatocytes + HBV 5:
- Rat CA2 Human hepatocytes + HBV 6:
- Rat CA3 Human hepatocytes 7:
- Rat CA4 Human hepatocytes
- Rat CA5 HBV
- 10: Rat CA6 HBV 11: Rat CA7 Saline

FIG.12

Hepatocytes plus HBV

1 week

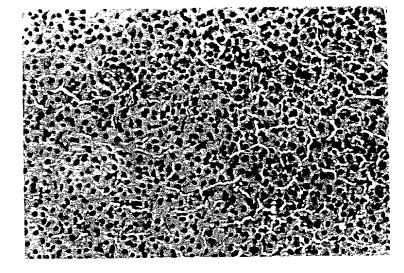


FIG.13A

Hepatocytes plus HBV

6 weeks

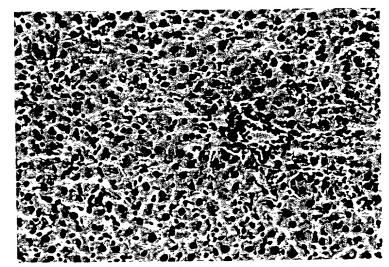


FIG.13B

Hepatocytes plus HBV

14 weeks

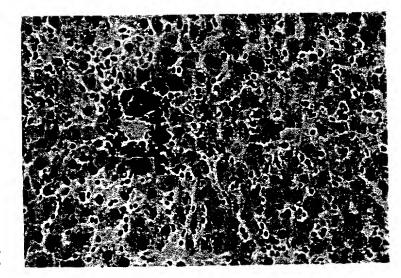


FIG.13C

Hepatocytes plus HBV

1 week

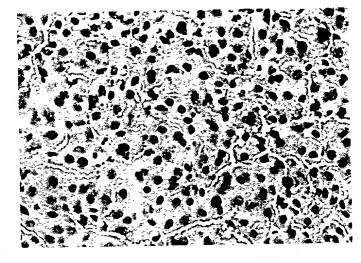


FIG.14A

Hepatocytes plus HBV

6 weeks

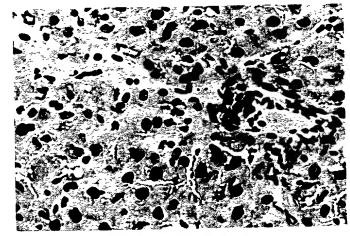


FIG.14B

Hepatocytes plus HBV

14 weeks

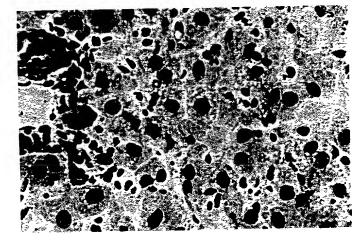
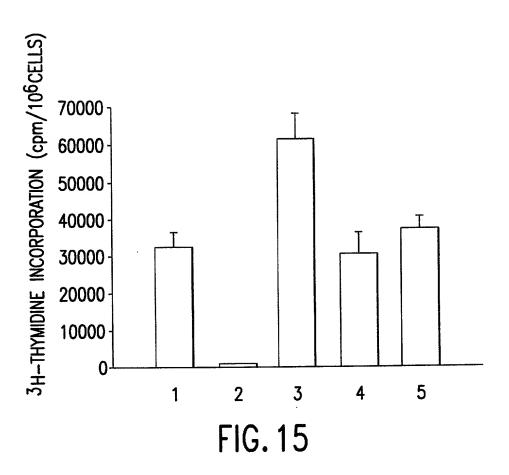


FIG.14C



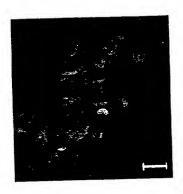


FIG.16A

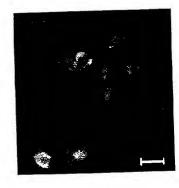


FIG.16B

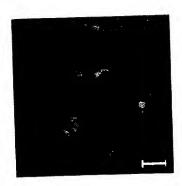


FIG.16C

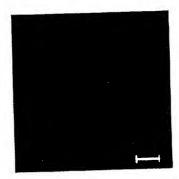


FIG.16D

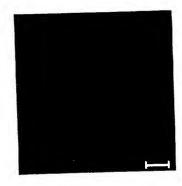


FIG.16E

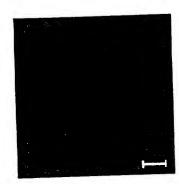


FIG.16F

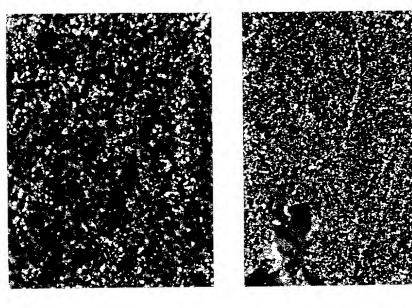


FIG.17A

FIG.17B

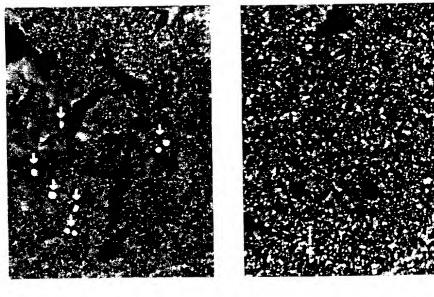


FIG.17C

FIG.17D

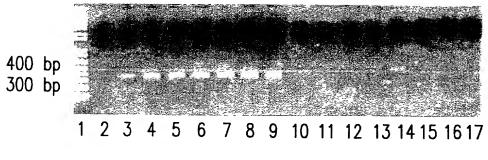


FIG.18A

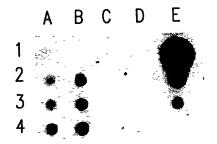
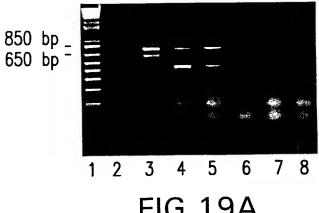
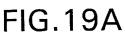
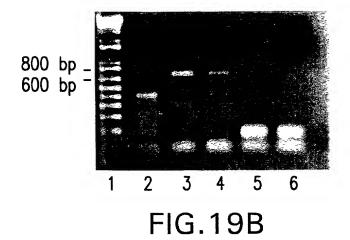
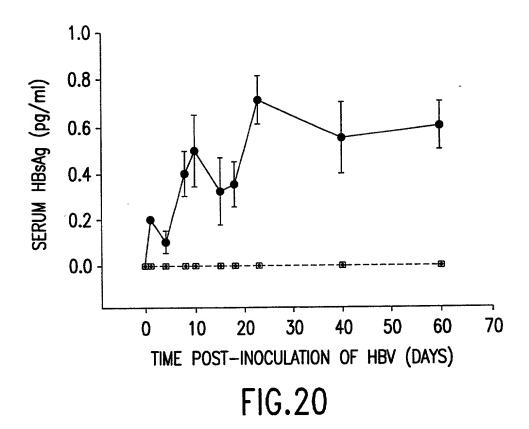


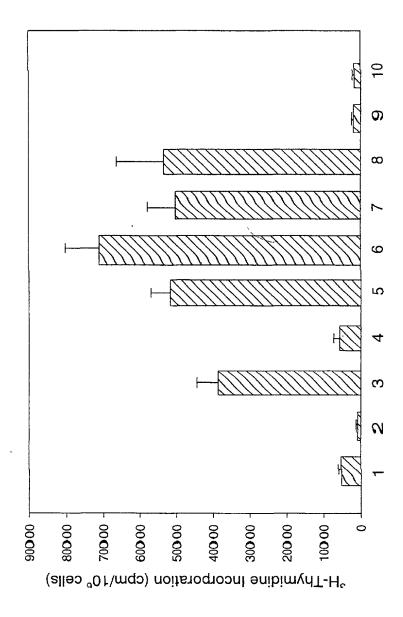
FIG.18B





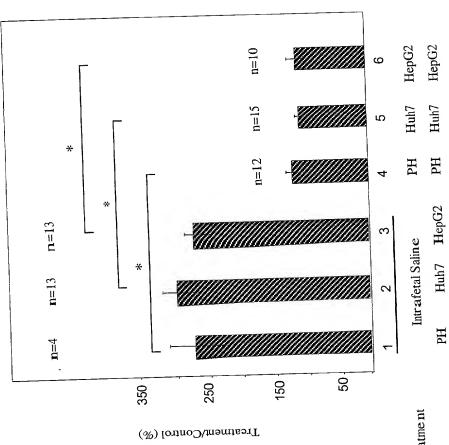




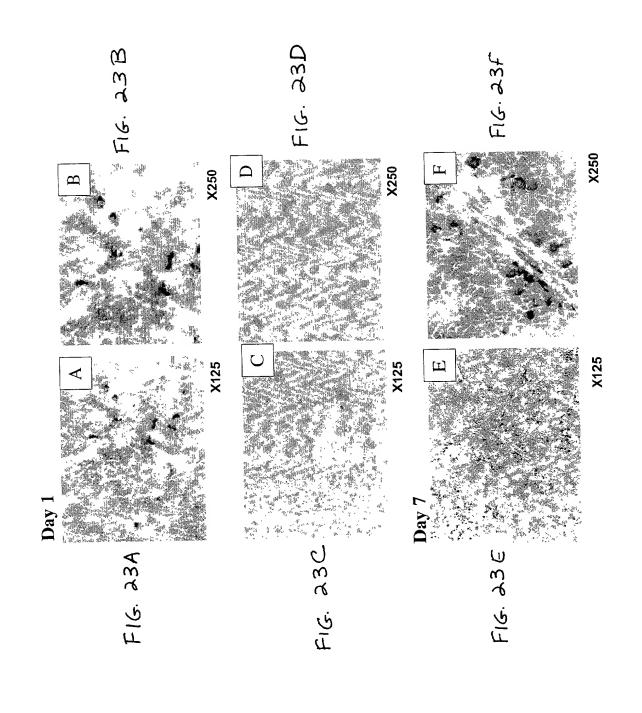


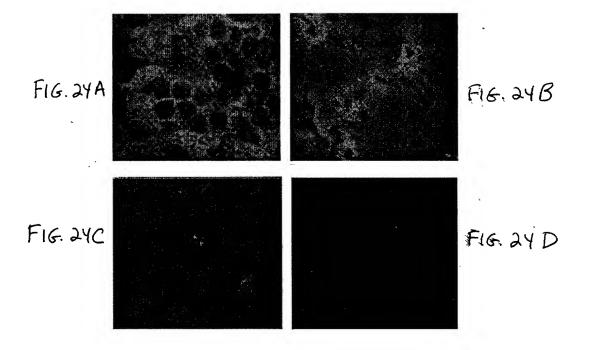
10 71出

77 91H



Responder Cell Source Treatment Stimulator Cells





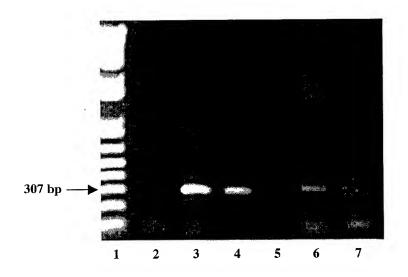


FIG. 25

FIG. 26A

Primary human hepatocytes

6 wks 16 wks

Tolerized and transplanted

Tolerized but not transplanted

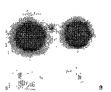
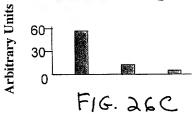


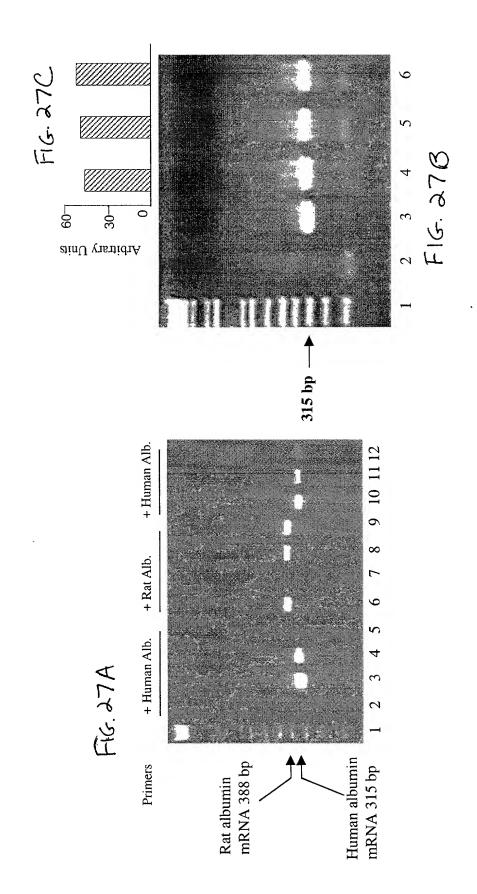
FIG. 26B

palb3 plasmid

100 pg 10 pg 1 pg







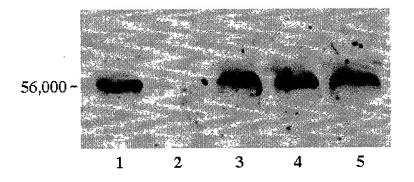


FIG. 28

duman Albumin

FIG. 29A

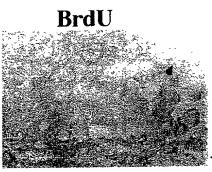


FIG. 29B

Tolerized with T3 no transplantation



FIG. 29C

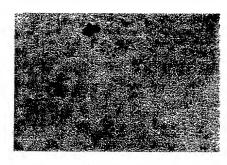


FIG. 29D



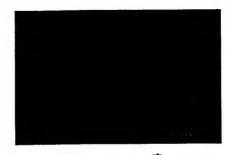


FIG. 29 E

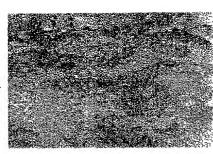


FIG. 29 F

Control no T3 no transplantation



161 nt

100 fg 10 fg 1 fg 0.1 fg 100 bp ladder FIG. 30

		Time Pc	Time Post-HCV Inoculation (weeks)	lation (weeks)		
	2	4	9	∞	12	16
Huh7	+	+	+	+	+	+
HepG2	+		. 1			F1G
PHH	+	+	1		L	31
PBS	+				E .	1

FIG. 32

